What is the function of the C1-C3 adrenergic group in the medulla?

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Abstract

This brief communication discusses a much neglected topic in functional neuroanatomy—the possible function(s) of the adrenergic system in the brain.

This brief communication discusses a much neglected topic in functional neuroanatomy—the possible function(s) of the adrenergic system in the brain. There are four aminergic neuromodulatory systems in the brain: these use dopamine, norepinephrine, serotonin and adrenaline[1]. There is a vast literature about the first three, but very little work has been done on the fourth, that has achieved a Cinderella status amongst the brain's neuromodulators. It is certainly a phylogenetically very primitive system, since its C1-C3 cell bodies are located in a more primitive location—the medulla—than the others, which have their cell bodies higher up in the pons, midbrain and basal forebrain. It has merely been assumed, without much evidence, that it may be restricted to low-level functions, such as cardiac and respiratory control. However, its neuroanatomical connections suggest something more interesting in addition. These nuclei have extensive rostral projections that reach as far up as the thalamus, and, more particularly from our present point of view, to the nuclei of all the other neuromodulators—substantia nigra (dopamine)[2]; the locus coeruleus (NE)[3]; the raphe nucleus (5-HT)[4]; and the lateral dorsal tegmental nucleus (cholinergic)[5]; as well as to key limbic structures, such as the hypothalamus[6]; the central tegmentum[7]; the periaqueductal grey[8,] and the midline paraventricular nucleus

of the thalamus[9]. It is difficult to see why a system, that is supposed to control only low-level functions, such as heart rate and blood pressure, would need this extensive projection to many of the key higher areas of the limbic system that is concerned *inter alia* with emotion.

The neuromodulatory system in the brain is not only exceedingly complicated but is also densely anatomically and physiologically interlinked, so that a primary disturbance in one system soon affects several other systems. However, it is not the purpose of this paper to review this extensive literature, but to spotlight one previously neglected area. The most basic behaviour exhibited by unicellular organisms is attraction (to food and safety) and repulsion (from danger). As organisms get more complex and develop nervous systems, this basic approach/flee dichotomy becomes elaborated and mediated by specific neurochemical mechanisms. In higher brains, behaviours of this kind are mediated anatomically by the limbic system, and neurochemically by the neuromodulator system.

Under normal circumstances this attract/repel—approach/flee mechanism fluctuates on either side of a neutral norm. Approach behaviour is associated with positive emotions and positive cognition, particularly when reinforced by consumatory input. Retreat behaviour is associated with negative emotions (particularly fear), especially is associated with the advent of painful stimuli. The control of approach/escape behaviours is mediated by extremely complex interactions between the neurotransmitters dopamine, norepinephrine, serotonin and acetylcholine[1]. In these reactions in humans, behaviour, emotion, and

ideation are all integrated into a prevailing mood. This integration could be effected by mutual interactions between the main neuromodulatory systems. Or there could be a master control —the conductor of this orchestra so to speak. The adrenergic system is well placed and well connected to act as the putative conductor of this orchestra, just as the cholinergic pedunculopontine and lateral dorsal tegmental nuclei in the pons and midbrain orchestrate consciousness in the brain[10], so the even more fundamental C1-C3 adrenergic nuclei in the medulla could orchestrate the basic behaviours of approach and retreat, with all their emotional and cognitive accompaniments. Disorders of this system could play a role in mood disturbances such as bipolar disorder. Further research on this neglected system seems indicated.

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